

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 25-27, 46, 55, 57, 59, 66 and 69-71 are pending in the application, with claims 27 and 46 being the independent claims. Claims 66, 70 and 71 have been withdrawn from consideration by the Examiner as being drawn to a nonelected invention. Claims 25-27, 46 and 66 are sought to be amended. Support for the newly added limitation in claim 46 can be found, *inter alia*, at page 25, lines 4-6 of the application as filed. Claims 56, 58, 61-65, 67, 68 and 72-75 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Numbering of Claims

Applicants note with appreciation that the Examiner has renumbered the claims submitted in Applicants' Amendment and Reply that was filed on November 21, 2002. *See* Office Action, page 2, lines 9-15.

In view of 37 C.F.R. § 1.114, Applicants further note that two claims that were sought to be added in Applicants' Amendment and Reply that was filed on September 6, 2001, have not been entered by the Examiner and are not included in the present numbering

of the pending claims. Applicants do *not* request entry of these two claims, because the scope of these two claims is congruent with the scope of pending claims 70 and 71.

II. Status of the Application

The Examiner has stated that:

Based on the election made in Paper No. 6, claims 25-27, 46, 55, 57-59, 61, 62, 64, 65, 68, 69 and 72 will be examined to the extent they read on the elected species and variants thereof (i.e., compounds wherein R₃ is -C(O)-CH₂-Y-G or -C(O)-CH₂-O-D). Claims 63, 66, 67, 70, 71 and 73-75 stand withdrawn from further consideration as being drawn to a nonelected invention.

Office Action, page 2, line 17, through page 3, line 2. Applicants respectfully disagree with the Examiner's analysis and conclusions.

In the Office Action, mailed on September 9, 1999 (Paper No. 3), the Examiner required election/restriction to one of eight perceived inventions. Only the first two perceived inventions were directed to chemical compound claims:

- I. Claims 1, 2, 25-29 and 46-57, drawn to compounds and compositions classified in class 552, subclass 500+.
- II. Claims 1, 2, 25-28 and 46-57, drawn to compounds and compositions classified in class 540, subclass 3+.

See Paper No. 3, page 2, lines 3-7.

As a preliminary matter, Applicants note that claims 63, 67 and 71-75 have been canceled.

In reply to Paper No. 3, Applicants elected, with traverse, the claims of group II. *See* Applicants' Reply to Restriction Requirement, first paragraph, filed November 9, 1999.

Compounds and compositions of class 540, subclass 3+, encompass compounds (and compositions thereof) having a cyclopentanohydrophenanthrene ring system containing heterocyclic carbon compounds containing a hetero ring having chalcogen (i.e., oxygen sulfur, selenium or tellurium) or nitrogen as the only ring hetero atoms. Further subclassifications includes, *inter alia*, compounds (and compositions thereof) wherein a nitrogen containing hetero ring is attached indirectly to the cyclopentanohydrophenanthrene ring system by nonionic bonding and wherein an oxygen containing hetero ring is attached indirectly to the cyclopentanohydrophenanthrene ring system by nonionic bonding. See U.S.P.T.O Classification Manual, class 540, subclasses 1, 2, 107 and 114.

Thus, Applicants' election of Group II encompasses not only compounds and compositions wherein R_3 is $-C(O)-CH_2-Y-G$ or $-C(O)-CH_2-O-D$ (as asserted by the Examiner in the quotation directly above) but also compounds and compositions wherein R_3 is $-C(O)-CH_2-Z-G$ (and G is C-attached heteroaryl or a quaternary ammonium salt of a nitrogen containing heteroaryl group). Furthermore, and for the same reasons, Applicants' election of Group II encompasses compounds wherein R_3 is $-C(O)-CH_2-Y'-Z-G$ (and G is C-attached heteroaryl or a quaternary ammonium salt of a nitrogen containing heteroaryl group).

Claim 66 is directed to: "The compound of claim 46, wherein R_3 is $-C(O)-CH_2-Z-G$, and G is C-attached heteroaryl or a quaternary ammonium salt of a nitrogen containing heteroaryl group." For the reasons given above claim 66 is within the scope of Applicants' elected invention.

Claim 70 is directed to: "The compound of claim 46, wherein R_3 is $-C(O)-CH_2-Z-G$." Claim 71 is directed to: "The compound of claim 46, wherein R_3 is $-C(O)-CH_2-Y'-Z-G$. In

claim 46, " G is one of C-attached heteroaryl, or a quaternary ammonium salt or N-oxide of a nitrogen containing heteroaryl group." For the reasons given above, claims 70 and 71 are within the scope of Applicants' elected invention.

For the reasons given above, Applicants' respectfully submit that claims 66, 70 and 71 are within the scope of Applicants' elected invention. Consequently, Applicants request that claims 66, 70 and 71 be rejoined for prosecution in the present application.

III. Claim Objections

The Examiner has objected to claims 25, 26 and 65 under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Examiner has required that these claims be canceled, amended to proper dependent form, or rewritten in independent form. Office Action, page 3, lines 6-8. Applicants respectfully traverse these objections.

In particular, the Examiner states that:

The instant claims recite R₃ is "-C(O)-CH₂-O-E". However, the parent claim 46 does not include said limitation and, thus, the instant claims are of improper dependent form.

Office Action, page 3, paragraph number 5, lines 5-7. Applicants respectfully disagree.

In the interest of advancing the prosecution of this application, claims 25 and 26 have been amended to delete the term "-C(O)-CH₂-O-E". Claim 65 has been canceled. Applicants respectfully submit that the Examiner's objections to claims 25, 26 and 65 have been accommodated and should be withdrawn.

IV. Rejection Under 35 U.S.C. § 112

Claims 25, 26, 46, 55, 57, 59, 64, 68 and 69 were rejected under 35 U.S.C. § 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Office Action, the paragraph bridging pages 3 and 4. Applicants respectfully traverse this rejection.

In particular, the Examiner states that:

The instant claims recite "G" or "D" can be "a N-oxide of a nitrogen containing heteroaryl group". The present specification lacks description of the instantly claimed subject matter and, thus, does not convey to the skilled artisan that applicant, at the time the application was filed, had possession of the claimed invention.

Office Action, page 4, lines 3-6. Applicants respectfully disagree.

In the interest of advancing the prosecution of the application, the term "or an N-oxide" has been deleted from independent claim 46. Claims 25, 26, 55, 57, 64, 68 and 69 are directly or indirectly dependent upon claim 46; and none recite the phrase "or an N-oxide." Applicants respectfully submit that the Examiner's rejection of 25, 26, 46, 55, 57, 64, 68 and 69 under 35 U.S.C. § 112, first paragraph, has been accommodated and should be withdrawn.

Claim 59 is directed to: "A pharmaceutical composition comprising a compound of claim 27 and a pharmaceutically acceptable carrier." Support for claim 59 can be found, *inter alia*, at page 29, line 7, through page 30, line 9, of the application as filed. Independent claim 27 is directed to a compound selected from a group of compounds, each of which is exemplified in the application as filed. Furthermore, claim 59 does not recite that G or D

can be an N-oxide of a nitrogen containing heteroaryl group (nor does independent claim 27, from which claim 59 directly depends). Thus, the specification does describe Applicants' claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully submit that the rejection of claim 59 under 35 U.S.C. § 112, first paragraph, has been overcome and should be withdrawn.

V. Rejections Under 35 U.S.C. § 103

A. Legal Principles

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's own disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

M.P.E.P., page 2143, lines 5-18.

B. *Bolger et al.*

The Examiner has maintained the rejection of claims 25-27, 46, 55, 57-59, 61, 64 and 65 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,232,917 (*Bolger et al.*). In addition, claims 69 and 72 were rejected under 35 U.S.C. § 103(a) over *Bolger et al.* Office Action, page 4, lines 10-12. Applicants respectfully traverse these rejections.

In particular, the Examiner states:

Applicant argues the reference does not exemplify any compounds wherein the C-21 position is substituted by either aryloxy or heteroaryl. Applicants's argument was considered but [found to be] not persuasive for teh following reason.

A reference is evaluated based on what it teaches the skilled artisan in the art at the time of the invention and not just on what is exemplified. The reference teaches (a) an equivalent between various 21-oxy substituents, (b) that R16 can be C₃-C₁₀ heterocyclic radical (see col. 8, lines 1-16) and (c) heterocyclic radicals such as oxazole, pyridine, pyrrole, pyrimidine and thiazole (see col. 11, lines 8-19). Therefore, making any of the exemplified compounds wherein the C-21 is substituted by a heteroaryloxy would be *prima facie* obvious. The motivation to make other species as taught by the reference is based on the desire to make additional compounds useful as taught by *Bolger*.

Office Action, page 4, line 13, through page 5, line 4. Applicants respectfully disagree.

Applicants incorporate by reference the argument presented in the Amendment and Reply Under 37 C.F.R. § 1.116, that was filed on November 21, 2002. With regard to the Examiner's rebuttal as quoted above, Applicants make the following additional remarks.

Bolger et al. discloses a vast Markush group of compounds (*see, e.g.*, col. 5, line 49, through, col. 11, line 19). For the Examiner to begin with the disclosure of *Bolger et al.* and

arrive at Applicants' claimed invention, requires at least two steps. First, the Examiner must select the proper subsets of the Markush group of Bolger *et al.* so that the group in the 17-position (the R₈ group of Bolger *et al.*) is a -C(O)-CH₂-O-(substituent) moiety. Second, the Examiner must select a substituent for the oxygen atom bonded to the 21-position.

Applicants submit that the Examiner has not established a *prima facie* case that it would be obvious to one of ordinary skill in the art to make the two successive selections necessary to begin with the disclosure of Bolger *et al.* and arrive at Applicant's claimed invention. Furthermore, Applicants submit that the Examiner has not established a *prima facie* case that it would be obvious to one of ordinary skill in the art to select from the myriad of heterocycles disclosed in Bolger *et al.* to arrive at the preferred embodiments as claimed by Applicants in claim 46. Therefore, claim 46 is not obvious in view of Bolger *et al.* As a preliminary matter. Claims 58, 61, 64 and 65 have been canceled. Claims 25-27 and 59 are directly or indirectly dependent on claim 46. Since it has been demonstrated above that independent claim 46 is not obvious in view of Bolger *et al.*, dependent claims 25-27 and 59 are also not obvious in view of Bolger *et al.*

For the reasons given above, Applicants respectfully submit that the Examiner's rejection of claims 25-27, 46, 55, 57-59, 61, 64 and 65 under 35 U.S.C. § 103(a) has been overcome and should be withdrawn.

C. *Phillipps et al.*

The Examiner has rejected claims 25-27, 46, 55, 57-59, 61, 62 and 68 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 3,959,260 (*Phillipps et al.*). Office Action, page 5, lines 9 and 10. Applicants respectfully traverse this rejection.

In particular, the Examiner states:

The instant claims differ from the reference by reciting compounds not exemplified by the reference. However, the reference teaches R³ may be a carbon-attached saturated or unsaturated heterocyclic group, such as pyridyl, morpholinyl (see especially col. 3, lines 36-40). Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including that of the instant claims, because an ordinary artisan would have the reasonable expectation that any of the species of the genus would have similar properties and, therefore, the same use as the genus as a whole. For example, it would have been obvious to the skilled artisan to modify the compound of example 40 by substituting the 21-(pyrid-2ylthio) group with any 21-heterocyclicthio group with the reasonable expectation that the compound produced would be useful as taught by [the] reference. The motivation to make other species as taught by the reference is based on the desire to make additional compounds having anaesthetic properties.

Office Action, the paragraph bridging pages 5 and 6. Applicants respectfully disagree.

Phillipps et al. teaches 21-acetylthio-3 α -steroids with variable pharmacological activity. For example, "21-[a]cetylthio-3 α -hydroxy-5 β -pregnane-11,20-dione is however a known compound but it is known to give highly undesirable side effects when administered as a suspension. . . . It is surprising that other 21-thio derivatives should exhibit such marked and useful activity." *Phillipps et al.*, col. 1, lines 52-60.

In the interest of expediting prosecution, the claims have been amended to render moot this rejection. The claims as presently amended do not read on 21-thioacetyl-3 α -

hydroxy-steroids.

For the reasons given above, Applicants respectfully suggest that the Examiner's rejection of claims 25-27, 46, 55, 57-59, 61, 62 and 68 under 35 U.S.C. § 103(a) as being obvious in view of Phillipps *et al.* has been overcome and should be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

Sterne, Kessler, Goldstein & Fox p.l.l.c.



Bruce E. Chalker
Attorney for Applicants
Registration No. 47,480

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600